Asian Journal of Pharmaceutical and Clinical Research

Innovare Academic Sciences
Knowledge to Innovation

Vol 17, Issue 8, 2024

Online - 2455-3891
Print - 0974-2441

Research Article

COMPARISON OF EPICARDIUM ADIPOSE TISSUE THICKNESS IN TREADMILL TEST POSITIVE AND NEGATIVE PATIENT

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Received: 21 May 2024, Revised and Accepted: 05 July 2024

ABSTRACT

Objective: The objectives of this study were as follows: (1) To find out the relationship between the epicardial adipose tissue (EAT) thickness and the treadmill (TMT) test results. (2) To find out the correlation between the EAT thickness and waist circumference and serum low-density lipoprotein-cholesterol.

Methods: This study was conducted on 77 patients with complaints of chest pain and came for evaluation to our institution during the study period. All the patients were explained about the study, transthoracic echocardiography, and about EAT as newer cardiovascular risk factors. After obtaining their verbal consent to participate in the study, a voluntary written informed consent was obtained from the patient and/or his/her legally acceptable representative.

Results: Majority of the patients were in the age group 41–50 years. Males (54.5%) were more in our study compared to the females. Out of the 77 patients with chest pain, who underwent TMT test, the test was positive in 50.6% patients, negative in 42.9% patients, and inconclusive in 6.5% patients. The comparison of fat pad thickness during the systole was found significantly higher in TMT-positive patients and lowest in the inconclusive patients ($p<0.05$).

Conclusion: There was a significant relationship between the TMT results and the EAT thickness in our study. The thickness of EAT was highest in TMT-positive patients and lowest in the TMT inconclusive test result patients.

Keywords: Epicardium, Adipose tissue, Treadmill test, Epicardial adipose tissue, Treadmill.

 DOI: http://dx.doi.org/10.22159/ajpcr.2024v17i8.51993. Journal homepage: https://innovareacademics.in/journals/index.php/ajpcr

INTRODUCTION

Epicardial adipose tissue (EAT) is novel cardiovascular risk factor. EAT produces proinflammatory and proatherogenic cytokines [1]. Various genes associated with extracellular matrix remodeling, inflammation, infection, and thrombosis pathways are linked to EAT [2]. Inflammatory cells are involved in plaque breakup through matrix degrading metalloproteinases as well as thrombosis following plaque disruption through the tissue factor pathway [3]. Tumor necrosis factor, monocyte chemoattractant protein 1, interleukin 1, interleukin 6, nerve growth factor, leptin, resistin, plasminogen activator inhibitor 1, and angiotensinogen, particularly white blood cell, play critical roles in this process [4]. EAT is found mostly along the major coronary arteries and branches in the atrioventricular and interventricular grooves, as well as in the atrium, right ventricle, and left ventricular free wall, and extends to the apex [5]. EAT has a similar embryological origin to intra-abdominal visceral adipose tissue [6]. Previous research has found that EAT is a higher risk factor for coronary artery disease (CAD) than adipose tissue from other regions of the body, and that EAT may play a key role in the progression of CAD [7-10]. Obesity is a major contributor to the development of atherosclerotic cardiovascular disease. The fat formed around the internal organs, known as visceral adipose tissue, is a sign for cardiovascular disease [11,12]. The visceral fat tissue EAT is a real visceral fat tissue. The previous studies have found a substantial link between abdominal fat accumulation and EAT. This was corroborated by the common embryogenesis pathway, which showed that epicardial fat and intra-abdominal fat in infancy were both brown adipose tissue. This adipose depot is now recognized as a source of bioactive molecules that may impact the coronary arteries, including as adiponectin [13], tumor necrosis factor-alpha, monocyte chemotactic factor-1, interleukin-1-beta, interleukin-6 [14], and inflammatory cytokines. There is a significant correlation between EAT thickness with abdominal visceral adipose tissue, age, waist circumference, body mass index, C-reactive protein, and homeostasis model assessment score. In participants with CAD, the thickness of EAT was greater than in those who did not have CAD. In patients with unstable angina, the thickness of EAT was greater than in those with stable angina or atypical chest pain. An EAT of >3.0 mm was found to be an independent risk factor for CAD [15]. Another study showed that EAT thickness was found to increase with the severity of CAD (multivessel more than single-vessel disease). They found that EAT of >5.2 mm can predict the CAD and has a sensitivity of 85% and specificity of 81% [16]. Treadmill (TMT) uses the electrocardiographic response to cardiopulmonary stress; blood pressure response; and workload, heart rate, and the blood pressure achieved at peak exercise. These indicators confirm the presence or absence and extent of the CAD when seen along with the clinical factors. A study from India reported a higher vessel involvement in TMT-positive patients. The sensitivity was 61% and specificity was 69% for the detection of the CAD in women, concluding that TMT test effectively diagnosed the CAD [17]. There is lacunae in the literature regarding the relationship between TMT test positivity and thickness of EAT. Hence, we had undertaken the present research work to compare the thickness of EAT with the TMT test results and also to find out the relationship between EAT thickness with low-density lipoprotein (LDL)-cholesterol level.

Objectives

The objectives of this study were as follows:

1. To find out the relationship between the EAT thickness and the TMT test results

2. To find out the correlation between the EAT thickness and waist circumference and serum LDL-c.

METHODS

This prospective cross-sectional observational study was done at Department of Medicine, MGM Medical College and M.Y. Hospital, Indore. Seventy-seven patients undergoing TMT for the evaluation of chest pain, followed by transthoracic echocardiography for estimation of EAT thickness and willing to provide their voluntary consent for participation in the study were included in the study.

Inclusion criteria

- Patients who are coming for TMT test in MY hospital for chest pain evaluation
- Patient and/or his/her legally acceptable representative willing to provide their voluntary written informed consent for participation in the study.

Exclusion criteria

- Patient and/or his/her legally acceptable representative not willing to provide their voluntary written informed consent for participation in the study
- Prisoners
- Pregnant females
- Patients <18 years of age
- Patients with psychiatric illness
- Patient with proven CAD
- Patient not fit for TMT test.

Methodology

All the patients were explained about the study, transthoracic echocardiography, and about EAT as newer cardiovascular risk factors. After obtaining their verbal consent to participate in the study, a voluntary written informed consent was obtained from the patient and/or his/her legally acceptable representative. All the study-related procedures were conducted after obtaining the consent. All included patients underwent thorough brief medical history and general medical examination. After that, electrocardiogram and lipid profile investigations were done. The study patients were taken for TMT test and results of the TMT test were noted. The results were categorized as positive, negative, and inconclusive. And after the TMT test, A Vivid S5 system (GE Vingmed Ultrasound AS, Norten, Norway) with a 2.5 MHz phased-array transducer was used to perform transthoracic echocardiography in the left lateral decubitus position. Transthoracic echocardiographic examinations were done by an experienced echocardiographer. Left ventricular ejection fraction was determined using modified Simpson's method [18]. EAT was defined as an echo-free gap between the myocardium and visceral pericardium that was measured perpendicularly on the free wall of the right ventricle at end diastole in three cardiac cycles from both parasternal long-axis and short-axis views [19]. Each site's maximum values were measured, and the average value was chosen.

Ethical committee approval was taken before start the study.

Data collection and methods

A customized pro forma was designed for the specific requirement of the study. All the information was collected in this customized pro forma.

Outcome measures

EAT thickness and results of TMT test were our outcome measures.

Statistical analysis

The data were initially captured in the customized pro forma and then transferred to Microsoft Excel for analysis. Descriptive statistics was presented in the form of numbers and percentages. For calculating p values, online statistical software such as GraphPad and Epi Info were used. Comparison of mean between more than two groups was done using one-way analysis of variance followed by *post-hoc* Tukey test. $p<0.05$ was taken as statistically significant.

OBSERVATION AND RESULTS

The above table shows the distribution of patients according to age. Twenty-two (28.6%) patients were in the age group 21–40 years, 37 (48.1%) were in the age group 41–60 years, and 18 (23.4%) were in the age group >60 years. Majority of the patients were in the age group 41–60 years.

The above table shows the distribution of patients according to sex. Thirty-five (45.5%) were female and 42 (54.5%) were male. Males were more in comparison to the females.

The above table shows the distribution according to TMT results. In 39 (50.6%), TMT was positive, in 33 (42.9%), TMT was negative, and in 5 (6.5%), TMT was inconclusive.

The above table shows the comparison of mean fat pad thickness (systole) in relation to TMT results. The mean fat pad thickness in systole in the TMT-positive patients was 5.91±1.86 mm, in TMT-negative patients was 3.59±1.94 mm, and in inconclusive patients, it was 3.60±1.72 mm. The comparison of mean fat pad thickness in relation to TMT results was found to be statistically significant (p=0.001) showing a varying fat pad thickness in relation to TMT results. The fat pad thickness was highest in TMT-positive patients and lowest in inconclusive patients. Pair-wise comparison was done using *post hoc* Tukey test.

The above table shows the comparison of mean fat pad thickness (diastole) in relation to TMT results. The mean fat pad thickness in diastole in the TMT-positive patients was 4.84±1.17 mm, in TMT-negative patients was 3.61±0.97 mm, and in inconclusive patients, it was 2.84±1.46 mm. The comparison of mean fat pad thickness in relation to TMT results was found to be statistically significant (p=0.001) showing a varying fat pad thickness in relation to TMT results. The fat pad thickness was highest in TMT-positive patients and lowest in inconclusive patients. Pair-wise comparison was done using *post hoc* Tukey test.

The above table shows the comparison of mean total cholesterol in relation to TMT results.

The mean total cholesterol in the TMT-positive patients was 105.97±24.74 mg/dL, in TMT-negative patients was 105.12±26.81 mg/dL, and in inconclusive patients, it was 96.60±23.29 mg/dL. The comparison of mean total cholesterol in relation to TMT results was found to be statistically not significant (p=0.743) showing a comparable total cholesterol among the TMT results.

The above table shows the comparison of mean high-density lipoprotein (HDL) cholesterol in relation to TMT results.

The mean HDL cholesterol in the TMT-positive patients was 22.74±5.01 mg/dL, in TMT-negative patients was 22.15±6.43 mg/dL, and in inconclusive patients, it was 21.40±4.72 mg/dL. The comparison of mean HDL cholesterol in relation to TMT results was found to be statistically not significant (p=0.834) showing a comparable HDL cholesterol among the TMT results.

The above table shows the comparison of mean LDL cholesterol in relation to TMT results.

The mean LDL cholesterol in the TMT-positive patients was 26.92±5.01 mg/dL, in TMT-negative patients was 27.73±6.21 mg/dL, and in inconclusive patients, it was 26.80±7.05 mg/dL. The comparison of mean LDL cholesterol in relation to TMT results was found to be statistically not significant (p=0.822) showing a comparable LDL cholesterol among the TMT results.

Table 1: Distribution of patients according to age

Age	Number	Percentage
21–40 years	22	28.6
41–60 years	37	48.1
>60 years	18	23.4
Total	77	100.0

Table 2: Distribution of patients according to sex

Sex	Number	Percentage
Female	35	45.5
Male	42	54.5
Total	77	100.0

Table 3: Distribution according to TMT results

TMT results	Number	Percentage
Positive	39	50.6
Negative	33	42.9
Inconclusive	5	6.5
Total	77	100.0

TML: Treadmill

Table 4: Comparison of fat pad thickness (systole) in relation to TMT results

TMT results	No.	Mean±SD	't' value	p-value
Positive	39	5.91±1.86	14.482	0.001*
Negative	33	3.59±1.94		
Inconclusive	5	3.60±1.72		
Total	77			

*One-way analysis of variance test applied. p<0.05 was taken as statistically significant. TML: Treadmill

Table 5: Comparison of fat pad thickness (diastole) in relation to TMT results

TMT results	No.	Mean±SD	"t" value	p-value
Positive	39	4.84±1.17	14.482	0.001*
Negative	33	3.61±0.97		
Inconclusive	5	2.84±1.46		
Total	77			

*One-way analysis of variance test applied. p<0.05 was taken as statistically significant. TML: Treadmill

Table 6: Comparison of total cholesterol in relation to TMT results

TMT results	No.	Mean±SD	"t" value	p-value
Positive	39	105.97±24.74	0.298	0.743, NS*
Negative	33	105.12±26.81		
Inconclusive	5	96.60±23.29		
Total	77			

*One-way analysis of variance test applied. p<0.05 was taken as statistically significant. TML: Treadmill

The above table shows the comparison of mean very-LDL (VLDL) cholesterol in relation to TMT results. The mean VLDL cholesterol in the TMT-positive patients was 30.56±6.14 mg/dL, in TMT-negative patients was 31.36±8.64 mg/dL, and in inconclusive patients, it was 26.20±6.30 mg/dL. The comparison of mean VLDL cholesterol in relation to TMT results was found to be statistically not significant (p=0.345) showing a comparable VLDL cholesterol among the TMT results.

Table 7: Comparison of HDL cholesterol in relation to TMT results

TMT results	No.	Mean±SD	"t" value	p-value
Positive	39	22.74±5.01	0.182	0.834, NS*
Negative	33	22.15±6.43		
Inconclusive	5	21.40±4.72		
Total	77			

*One-way analysis of variance test applied. p<0.05 was taken as statistically significant. HDL: High-density lipoprotein, TML: Treadmill

Table 8: Comparison of LDL cholesterol in relation to TMT results

TMT results	No.	Mean±SD	"t" value	p-value
Positive	39	26.92±5.01	0.197	0.822, NS*
Negative	33	27.73±6.21		
Inconclusive	5	26.80±7.05		
Total	77			

*One-way analysis of variance test applied. p<0.05 was taken as statistically significant. LDL: Low-density lipoprotein, TML: Treadmill

Table 9: Comparison of VLDL cholesterol in relation to TMT results

TMT results	No.	Mean±SD	"t" value	p-value
Positive	39	30.56±6.14	1.079	0.345, NS*
Negative	33	31.36±8.64		
Inconclusive	5	26.20±6.30		
Total	77			

*One-way analysis of variance test applied. p<0.05 was taken as statistically significant. TML: Treadmill, VLDL: Very-low-density lipoprotein

Table 10: Comparison of triglycerides in relation to TMT results

TMT results	No.	Mean±SD	"t" value	p-value
Positive	39	167.67±43.00	0.357	0.701, NS*
Negative	33	160.55±57.73		
Inconclusive	5	150.60±48.51		
Total	77			

*One-way analysis of variance test applied. p<0.05 was taken as statistically significant. TML: Treadmill

The above table shows the comparison of mean triglycerides in relation to TMT results. The mean triglycerides in the TMT-positive patients were 167.67±43.00 mg/dL, in TMT-negative patients was 160.55±57.73 mg/dL, and in inconclusive patients, it was 150.60±48.51 mg/dL. The comparison of mean triglycerides in relation to TMT results was found to be statistically not significant (p=0.701) showing a comparable triglycerides among the TMT results.

DISCUSSION

The present study was conducted to evaluate the EAT thickness who are tested positive or negative on TMT test in patients with chest pain. EAT, or EAT, is a new cardiovascular risk factor that produces proinflammatory and proatherogenic cytokines. Inflammatory cells are involved in plaque disintegration through matrix degradation metalloproteinases and thrombosis initiation through the tissue factor pathway. The thickness of EAT increases in patients with CAD, and it was higher in unstable angina patients compared to stable angina patients. A cutoff of EAT thickness of more than or equal to 3.0 mm has been reported to be an independent risk factor for CAD. There is higher vessel involvement in TMT-positive patients with a sensitivity and specificity of over 60% and this study concluded that TMT test is effective in diagnosing CAD. With this background, the present study was initiated in our institution to evaluate the EAT thickness in patients with TMT-positive test result. We had included 77 patients with chest pain coming to our Department of Medicine and undergoing evaluation of chest pain. These patients initially underwent TMT test and then underwent transthoracic echocardiography. Majority of the patients in our study were in the age group 41–60 years and 21–40 years. Males (54.5%) were more than females (45.5%). In 50.6% (39) patients, TMT was positive, in 42.9% (33) TMT was negative, and in 6.5% (5) patients TMT was inconclusive. The mean EAT thickness in systole in TMT-positive patients was 5.91±1.86 mm, in TMT-negative patients was 3.59±1.94 mm, and in TMT inconclusive patients was 3.60±1.72 mm. Comparison of mean EAT thickness was significantly higher in TMT-positive patients and significantly lower in inconclusive patients ($p=0.001$). Sinha *et al*. [20] compared the epicardial adipose thickness in patients with and without CAD. The epicardial adipose thickness was measured at end-systole. Higher EAT was associated with severe CAD and presence of multivessel disease ($p<0.05$). The mean EAT thickness in diastole in TMT-positive patients was 4.84±1.17 mm, in TMT-negative patients was 3.61±0.97 mm, and in TMT inconclusive patients was 2.84±1.46 mm. Comparison of mean EAT thickness was significantly higher in TMT-positive patients and significantly lower in inconclusive patients ($p=0.001$).

The mean EAT thickness during both systole and diastole was highest in TMT-positive patients and lowest in TMT inconclusive patients. In a study by Shambu *et al*. [21], mean EFT was significantly higher in patients with CAD compared to control group patients ($p<0.05$). Nabati *et al*. [22] found a significant correlation of epicardial fat thickness with severity of CAD ($p<0.001$). In a study by Ghaderi *et al*. [23], the mean epicardial fat thickness was significantly higher in CAD group compared to patients without CAD ($p<0.05$). Jeong *et al*. [24] showed significant correlation of severity of CAD with epicardial fat thickness ($p<0.05$). Lipid profile (total cholesterol, HDL cholesterol, LDL cholesterol, and VLDL cholesterol) was comparable among the TMT test results ($p>0.05$). In all the patients, the lipid parameters were similar in relation to TMT test results.

CONCLUSION

Our study conclude that, there was a significant relationship between the TMT results and the EAT thickness. The thickness of EAT was highest in TMT-positive patients and lowest in the TMT inconclusive test result patients. This was a preliminary attempt at understanding of the relationship between EAT thickness and the TMT results. This study provided us with a basis that EAT can be used for the marker of CAD in patients presenting with complaints of chest pain. We recommend a further large study to evaluate the number of vessels involved and the severity of CAD based on EAT thickness.

Limitation of the study

The limitation of our study is that we only evaluated the thickness of EAT thickness (EAT), but did not evaluate the relationship of EAT thickness with the severity of CAD and the number of vessels involved.

CONFLICTS OF INTEREST

None declared.

FUNDING

Nil.

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